Amendments to the Specification:

Please replace the paragraph at page 5, lines 21-31, with the following amended paragraph:

It is surprising that the treatment of cells infected with an intra-cellular pathogen with heat or tumour necrosis factor produces SPs which are more immunogenic than SPs derived from non-induced cells or cells which have been stressed by other stimuli. A notable aspect of immunity elicited by these induced SPs is the long-term memory compared to that induced by ~~immunisation~~ immunization by other SP subsets. The best memory responses for bacterial pathogens are seen with heat-induced stress proteins and for protozoan and parasitic pathogens with tumour necrosis factor.

Please replace the paragraph at page 10, line 19, with the following amended paragraph:

Preferably, the immunogenic determinant for the present invention is delivered in combination with an adjuvant. Suitable adjuvants are readily apparent to the person skilled in the art, such as Freund's complete adjuvant, Freund's incomplete adjuvant, ~~Quil-A~~ QUIL A™ (Quil A Saponin), Detox, ISCOMs or squalene. However, it will be appreciated that the vaccine of the present invention may also be effective without an adjuvant. Such a vaccine may be given by any suitable means, such as orally, or by injection.

Please replace the paragraph at page 10, lines 20-29, with the following amended paragraph:

It will be appreciated that specific immunogenic SP/antigenic peptide fragment complexes can be isolated from the mixture of complexes produced from the stressing of the cellular material to produce a vaccine with is pathogen specific. However, this will usually not be required and the mixture of complexes can be used to induce broad spectrum ~~immunisation~~ immunization. If desired, the specific antigenic peptide fragments can be recovered from the complex, for example by treatment with ATP using conventional techniques.

Please replace the paragraph from page 10, line 31, to page 11 line 7, with the following amended paragraph:

The SP/antigenic peptide fragment complex of the vaccine of the present invention may be delivered in combination with an adjuvant and in an aqueous carrier. Suitable adjuvants are readily apparent to the person skilled in the art, such as Freund's complete adjuvant, Freund's incomplete adjuvant, ~~Quil A~~ QUIL A™ (Quil A Saponin), Detox, ISCOMs or squalene. However, the vaccine compositions of the present invention may also be effective without an adjuvant.

Please replace the paragraph from page 11, line 28, to page 12 line 7, with the following amended paragraph:

The vaccines of the invention may contain any suitable concentration of the SP/antigenic peptide fragment complex. We prefer that the SP complex is administered in the range of 10-600 pg, preferably 10-100 pg, most preferably 25 pg, per Kg of body weight of the animal being treated. It will be appreciated that the vaccine of the invention may be applied as an initial treatment followed by one or more subsequent treatments at the same or a different dosage rate at an interval of from 1 to 26 weeks between each treatment to provide prolonged ~~immunisation~~ immunization against the pathogen.

Please replace the paragraph from page 12, line 25, to page 13 line 24, with the following amended paragraph:

Cells infected with M. Bovis were washed in a serum-free media, such as RPMI (Roswell Park Medical Institute) (Sigma), then heat-shocked at 45°C for 0.5hr or at 42°C for 5hr and cultured overnight. The cells are then washed in serum-free media, followed by a wash in phosphate

buffered saline (PBS). The cells are then re-suspended in homogenisation buffer. The homogenisation buffer may be a hypotonic buffer, such as 10 mM phosphate pH 7.4 with 2mM MgCl2, after which the cells are then disrupted using a cell homogeniser (e.g. a Dounce or Potter homogeniser, Ultraturrax or Waring blender). Alternatively, the homogenisation buffer may contain detergent, such as PBS with 0.5% Tween, the detergent concentration being between 0.1-1% and suitable to solubilise the cell membrane. The cell lysate is then treated by centrifugation, typically 3-5000g for 5 minutes, to remove the nuclei and cell debris, followed by a high speed centrifugation step, typically 100,000g for 15-30 minutes. The supernatant thus obtained is processed to give an SP/antigenic peptide fragment complex suitable for use in a vaccine. This can be done simply by ammonium sulphate precipitation which uses a 20-70% ammonium sulphate cut. Specifically, 20% (w/w) ammonium sulphate is added at 4°C, the precipitate is discarded, followed by the addition of more ammonium sulphate to bring the concentration to 70% w/w. The protein precipitate is harvested by centrifugation and then dialysed into an appropriate physiological, injectable buffer, such as saline, to remove the ammonium sulphate before use. It will be appreciated that the SP complexes isolated in this way are not purified to homogeneity, but are nevertheless suitable for use as a vaccine component.

Please replace the paragraph at page 15, lines 11-12, with the following amended paragraph:

Example 3: Immunization ~~Immunisation~~ with induced SPs; immunity in vaccine recipient:

Please replace the paragraph at page 15, lines 14-27, with the following amended paragraph:

SPs were prepared as described above and mice and rabbits were vaccinated with 1-10 micrograms of the stress-protein containing extract in phosphate buffered saline and boosted with identical vaccine dosages a month after the primary injection. Induction of immunity to pathogen was assayed by Western blot analysis using total plasmodium or M. bovis proteins. Antibody titres of 1: 1-10,000 were routinely obtained and cytotoxic T-cell activity directed

against pathogen infected cells could also be detected in the ~~immunised~~ immunized mice. Challenge of the rabbits with fixed plasmodium or M. bovis at 6,12 and 18 months periods after the initial ~~immunisations~~ immunizations resulted in the production of good antibody responses with titres of 1: 1-10 000 indicating good memory responses in the ~~immunised~~ immunized animals.

Please replace the paragraph from page 16, line 19, to page 17 line 9, with the following amended paragraph:

Associated peptides were eluted from the purified HSPs and SPs by re-suspending the precipitated complexes in 10% acetic acid and boiling for 15 minutes to dissociate the complexes. The denatured HSPs and SPs were pelleted in a Beckman airfuge for 30mins in a cold room and the peptide containing supernatants harvested by freeze-drying and analysed by capillary zone electrophoresis using a BeckmanCZE system. The CZE profiles of the peptides eluted from the constitutive and the TNF-induced M. Tuberculosis SPs and the HSPs were significantly different from each other as shown in Figs 1-3, indicating that all three types of SPs carried distinct families of associated peptides. Immunization ~~Immunisation~~ of rabbits with all three types of SPs showed similar antibody titres in animals ~~immunised~~ immunized with the constitutive and TNF-induced SPs compared to significantly higher antibody titres (10-50x) in animals ~~immunised~~ immunized with heat-induced bacterial SPs. Immunization ~~Immunisation~~ with admixtures of the eluted peptides and the denatured SPs or HSPs from which they were isolated gave poor antibody responses indicating that the immunity induced required native, intact SP-associated peptide complexes.

Please replace the paragraph from page 17, line 13, to page 18 line 1, with the following amended paragraph:

Rat liver hepatocytes were prepared by forcing collagenase digested PVG rat livers through a fine mesh sieve and washing the isolated cells by centrifugation through DMEM tissue culture media. Washed cells were re-suspended at a cell density of 7x106 cells/ml and infected with Plasmodium Berghei by co-culture at 37°C for 4hrs. Infected cells were used to prepare lysates for antibody titre assay, or cultured overnight in the presence or absence of lug/ml TNF-a at 37 C for the isolation of constitutive or TNF-induced SPs. Cells were pelleted by centrifugation at 3000g for 5 minutes and re-suspended in lysis solution of 1% Tween in 100mM Tris-HCl, pH8. The cell lysate was centrifuged at 5000g for 5 minutes to remove the nuclei and cell debris, followed by a high speed centrifugation step at 100,000g for 15-30 minutes. Cleared lysate was then used for antibody titre assays or to isolate SPs for ~~immunisation~~ immunization. Constitutive and TNF induced SPs were prepared from the cleared lysates by ammonium sulphate precipitation as described in Example 1 above.

Please replace the paragraph at page 18, lines 3-12, with the following amended paragraph:

Rabbits were ~~immunised~~ immunized with the SPs isolated from constitutive or TNF-induced and heat-induced bacteria resuspended in phosphate buffered saline without any added adjuvant in either the primary or booster vaccinations. Antibody titres in the ~~immunised~~ immunized animals were assayed by 10-fold serial dilutions using a dot-blot assay on total cell lysates prepared from freshly infected hepatocytes as described analysis above. Animals vaccinated with TNF induced SPs showed a 10 to 100 fold higher antibody titre than those ~~immunised~~ immunized with constitutive SPs.